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Comparative Effectiveness of Ramipril Versus Losartan in Adults with Primary Hypertension: A Scoping Review

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ABSTRACK

Hypertension remains one of the leading global risk factors for cardiovascular morbidity and mortality. Despite the availability of multiple antihypertensive drug classes, achieving optimal blood pressure control continues to be a major clinical challenge worldwide. This research aims to compare the efficacy of Ramipril and Losartan in the management of Primary Hypertension. This scoping review analyzed articles published between January 2006 and January 2026 from PubMed, ScienceDirect, OpenAlex, and DOAJ. Inclusion criteria included English-language observational studies addressing the efficacy of both antihypertensives. Four articles were selected after a rigorous screening process. Ramipril was more effective in reducing SBP and DBP, whereas Losartan was superior for EF and LV remodeling. Ramipril also increased GSH and total antioxidant status, while Losartan was more effective for metabolic and vascular remodeling biomarkers. Ramipril is commonly associated with adverse effects such as cough, whereas dizziness is more frequently reported with Losartan. Losartan has been shown to be more effective in hypertensive patients with left ventricular hypertrophy (LVH) and may also contribute to improvements in insulin resistance. Further head-to-head comparison studies are needed to guide optimal therapy.

Keywords: hypertension, adult, losartan, ramipril, sistolic blood pressure, diastolic blood pressure

INTRODUCTION

Primary hypertension, a common chronic illness, contributes significantly to adult cardiovascular morbidity and premature mortality. Hypertension is a leading cause of ischemic heart disease, stroke, and chronic kidney disease worldwide, placing a substantial burden on health systems, particularly in low- and middle-income countries (Mills et al., 2020). Despite the availability of modern medications, hypertension management remains inadequate for over a billion individuals (WHO, 2023).

RAAS inhibition is essential for foundational hypertension treatment. First-line antihypertensive agents include ACE inhibitors and ARBs, both of which reduce blood pressure and cardiovascular risk (Williams et al., 2018). ACE inhibitors, such as ramipril, and ARBs, such as losartan, an early ARB, are widely utilized in clinical practice due to their demonstrated efficacy and safety (Campbell et al., 2022; Chen et al., 2021).

Although both drug classes target the RAAS, they do so via distinct mechanisms. ARBs selectively block angiotensin II type 1 receptors without affecting bradykinin metabolism, whereas ACE inhibitors reduce angiotensin II and simultaneously enhance bradykinin activity (Alcocer et al., 2023; Smolińska et al., 2023; Taddei & Bortolotto, 2016). These mechanistic differences may influence adverse event profiles and rates of treatment discontinuation (Burnier & Egan, 2019). Long-term adherence is often higher with ARBs, which are generally better tolerated than ACE inhibitors (Messerli et al., 2018). ACE inhibitors can cause side effects such as cough and angioedema.

Both ARBs and ACE inhibitors produce comparable reductions in systolic and diastolic blood pressure in patients with primary hypertension, as demonstrated in randomized controlled trials and large meta-analyses (Xie et al., 2020). However, cardiovascular, renal, and safety outcomes may differ between the two drug classes (Brunström & Carlberg, 2018). Given their improved tolerability, ARBs may provide enhanced cardiovascular benefits in real-world populations (Ettehad et al., 2016).

Although ramipril and losartan are commonly prescribed, direct comparisons between the two are limited. Many antihypertensive studies focus on drug classes rather than individual agents, making agent-specific conclusions difficult to apply in clinical decision-making (Burnier, 2019). Variability in study design, patient demographics, and outcome measures underscores the need for a comprehensive literature synthesis. Ramipril and losartan are specifically compared in patients with primary

hypertension in this scoping review, which aims to summarize major findings and identify knowledge gaps relevant to clinical practice and antihypertensive optimization studies (Bruyn et al., 2022; Le et al., 2025; Rahman et al., 2024).

Several studies have demonstrated the effectiveness of treating hypertension with different drug classes, including ACE inhibitors and ARBs (Williams et al., 2018; Burnier & Egan, 2019). Research directly comparing ramipril and losartan as primary therapy for primary hypertension remains limited. Most studies evaluate ACE inhibitors versus ARBs at the class level, with few focusing on direct comparisons between these two agents (Xie et al., 2020). Available evidence generally indicates similar reductions in blood pressure with ramipril and losartan, though differences in adverse events and cardiovascular or metabolic outcomes highlight the need for further agent-specific research (de Boer et al., 2022; Hiremath et al., 2026).

Even when comparative studies exist, findings remain inconsistent regarding effects on systolic (SBP) and diastolic blood pressure (DBP) and long-term cardiovascular outcomes. This variability contributes to uncertainty in selecting the optimal agent for patients with primary hypertension, particularly in those with comorbidities such as left ventricular hypertrophy (LVH) or insulin resistance (Aqilla, 2025; Valerio et al., 2024; Wei, 2024).

This review addresses the existing gap by providing a comprehensive synthesis of the literature on the effectiveness of ramipril and losartan in managing primary hypertension. Its primary objective is to offer a direct comparison between these drugs, emphasizing their impact on SBP, DBP, cardiovascular outcomes, and metabolic parameters. The study also examines drug-specific adverse effects to aid clinicians in selecting therapy tailored to individual patient profiles.

The overall goal of this study is to compare the effectiveness of ramipril and losartan in managing primary hypertension, focusing on blood pressure reduction and improvements in cardiac and metabolic outcomes. Additionally, the study evaluates differences in side effect profiles, which may influence long-term therapy adherence. By providing rigorous evidence, this review aims to inform clinical decision-making, enhance patient outcomes, and reduce adverse events associated with antihypertensive therapy. Furthermore, the findings may improve understanding of hypertension management in populations with LVH or other metabolic disorders.

METHOD

Processing written materials, reading and recording them, and gathering library data as part of a literature study constituted the first steps in the data collection process. Topics covered in published articles or related publications were defined as data sources. A scoping review was the method used in this research.

The articles were evaluated according to population, intervention, comparison, and outcomes (PICO). In January 2026, a literature search was conducted for essential hypertension, ramipril, losartan, and diastolic blood pressure in adults aged 18 and older. This study employed secondary research methods. International publications on specific topics provided secondary data. We searched PubMed, ScienceDirect, OpenAlex, and DOAJ for English-language literature. The keywords used were:

("Hypertension, Essential"[Mesh] OR "essential hypertension"[tiab] OR "primary hypertension"[tiab]) AND ("Ramipril"[Mesh] OR ramipril[tiab]) AND ("Losartan"[Mesh] OR losartan[tiab]) AND ("Randomized Controlled Trial"[Publication Type] OR randomized[tiab] OR randomised[tiab]) AND (comparative[tiab] OR "head-to-head"[tiab] OR versus[tiab] OR vs[tiab]) AND ("Adult"[Mesh]) NOT (secondary hypertension[tiab] OR pediatric[tiab] OR child*[tiab]).

The inclusion criteria for the literature search comprised studies involving adult patients (≥18 years) diagnosed with primary hypertension, evaluating ramipril as the intervention and losartan as the comparator, and reporting outcomes related to changes in systolic blood pressure (SBP) and/or diastolic blood pressure (DBP). Eligible studies were randomized controlled trials employing either parallel or crossover designs, available in full-text format, written in English, and accompanied by abstracts. Additionally, the studies had to be published within the period from January 2006 to January 2026. Meanwhile, studies categorized as scoping reviews, literature reviews, or meta-analyses were excluded from this research.

During the first step of the article search (identification), 208 publications were located using the four data sources: PubMed, ScienceDirect, OpenAlex, and DOAJ. Of these, 25 were from

ScienceDirect, 77 from PubMed, 75 from OpenAlex, and 31 from DOAJ. After removing 59 duplicates, 149 items remained.

The second step, "screening," involved reviewing article titles and abstracts for relevancy to the literature review. Articles that did not meet the requirements were excluded. After this process, 121 articles were removed, leaving 28 that satisfied the initial screening criteria. Articles from scoping reviews, systematic reviews, and meta-analyses were excluded during the "eligibility" step. Additionally, only free full-text articles that addressed the effectiveness of ramipril versus losartan in adults with primary hypertension and met the inclusion criteria within the previous twenty years (January 2006–January 2026) were reviewed.

The final step, referred to as "inclusion," involved identifying the number of studies that fully met the inclusion and exclusion criteria and aligned with the objectives of this scoping review. Four studies satisfied all criteria, while the remaining twenty-eight were excluded. The flowchart below (Figure 1) summarizes the outcomes of the article selection process.

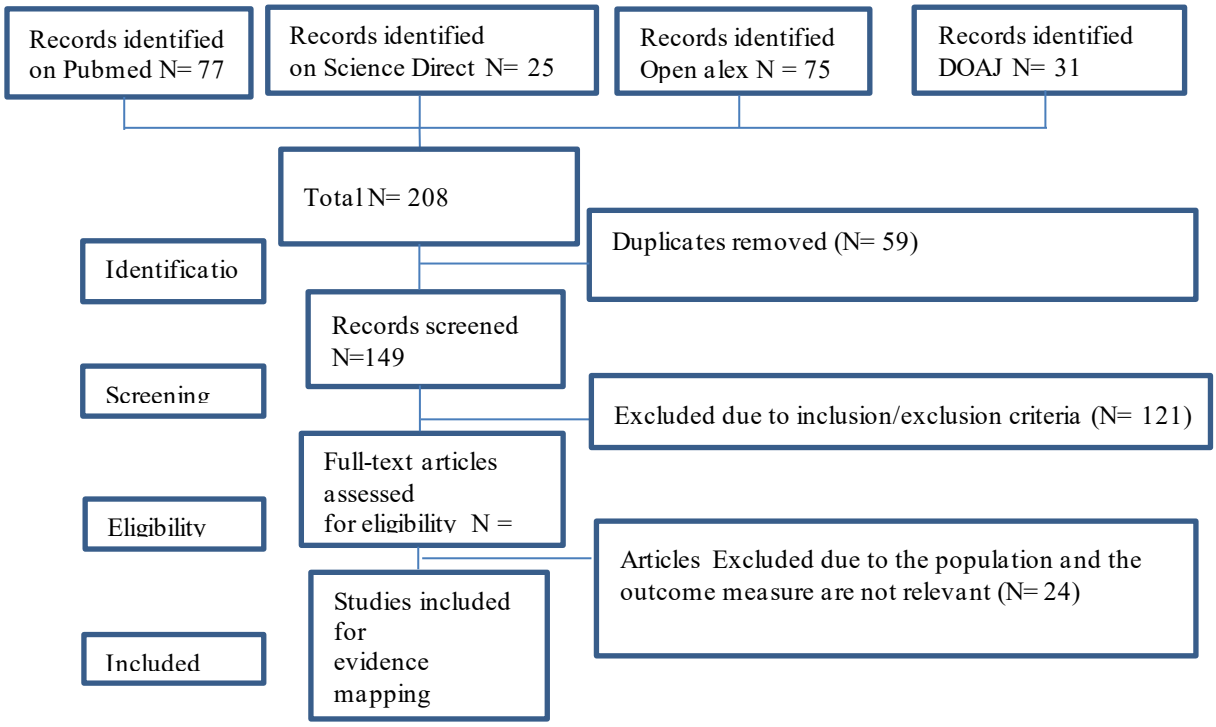

Figure 1. PRISMA-based flow diagram

Source: Adapted to article selection method adapted from the PRISMA guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analyses).

RESULTS AND DISCUSSION

Table 1. Comparative Effectiveness of Ramipril Versus Losartan in Adults With Primary Hypertension

No	Author – Year – Study Design	Sampel & Follow-up	Blood Pressure Outcome (SBP/DBP)	Key Findings
1	**Kaoser Alam et al., 2021** – Hospital-based prospective comparative study	120 patients with hypertensive heart failure (Ramipril n=60; Losartan n=60); 12 weeks	Ramipril: −28.4 ± 6.2 / −14.2 ± 3.1 mmHg; Losartan: −24.1 ± 5.8 / −13.8 ± 3.4 mmHg	Ramipril is more effective at lowering SBP; Losartan is superior to EF and LV remodeling; similar NYHA improvements; coughing more often on Ramipril
2	**Uday Kiran et al., 2010** – Comparative clinical	A total of 75 subjects (Losartan n=25; Ramipril	Ramipril: 165.1 ± 14.1 → 147 ± 15.2 / 94.2 ± 11.7 → 85.4 ± 8.4 mmHg;	Ramipril lowers blood pressure more significantly; increase

	study with healthy controls	n=25; healthy control n=25); 10 days	Losartan: 153 ± 11 → 140 ± 10.9 / 94 ± 11.9 → 91 ± 10.5 mmHg	antioxidant and NO status
3	**Giuseppe Derosa et al., 2011** – Randomized double-blind multicenter clinical trial	215 patients (Losartan n=108; Ramipril n=107); 14 months	Ramipril: 152 ± 10 → 127 ± 6/97 ± 8 → 79 ± 3 mmHg; Losartan: 152 ± 10 → 126 ± 5 / 97 ± 8 → 80 ± 4 mmHg	The decrease in SBP and DBP is similar; Losartan is superior in metabolic biomarkers and vascular remodeling
4	**Christiano Argano et al., 2006** – Randomized double-blind three-arm double-dummy trial	57 patients with stage 1–2 essential hypertension; 24 weeks	Losartan: 162 ± 7 → 133 ± 5/94 ± 6 → 82 ± 7 mmHg; Ramipril: 159 ± 7 → 134 ± 5 / 98 ± 9 → 81 ± 8 mmHg; Combination: 161 ± 8 → 131 ± 6 / 94 ± 12 → 78 ± 8 mmHg	All therapies are effective; The combination of Ramipril–Losartan provides the largest LVH regression

Source: Alam et al., 2021; Kiran et al., 2010; Derosa et al., 2011; Argano et al., 2006.

Among patients with primary (essential) hypertension, angiotensin-converting enzyme (ACE) inhibitors such as ramipril have demonstrated substantial efficacy in reducing systolic and diastolic blood pressure and in lowering the risk of long-term cardiovascular events through suppression of the renin–angiotensin–aldosterone system and improvement of vascular compliance (Yusuf et al., 2000; Messerli et al., 2018). ARBs, such as losartan, reduce blood pressure by inhibiting angiotensin II at the AT_1 receptor, lowering side effects such cough and angioedema (Burnier, 2001; Whelton et al.,

Major international guidelines recommend ramipril and losartan as first-line treatments for primary hypertension, but head-to-head comparisons have shown inconsistent results in lowering blood pressure and preventing cardiovascular outcomes, highlighting the need for more systematic and comparative studies (Williams et al., 2018).

Comparison of Effects on SBP and DBP

Other studies demonstrate Ramipril decreases SBP better than Losartan. Ramipril reduced SBP 28.4 mmHg comparison. One research found 24.1 for Losartan. Bradykinin potentiation and angiotensin II inhibition improve SBP control with ramipril (Alam et al., 2021; Kiran, 2010). Equal Effectiveness: Some studies show that both drugs decrease SBP and DBP equally (Agrano et al., 2006; Derosa, 2011). Both achieve large baseline reductions and normalize blood pressure (≤140/90 mmHg) (Agrano et al., 2006).

1) Ramipril

Pharmaceutical effects: Ramipril increases bradykinin and decreases peripheral vasoconstriction and aldosterone secretion by inhibiting ACE conversion from I to II (Messerli et al., 2018). Ramipril decreases blood pressure and improves endothelial function and vascular compliance in primary hypertension patients, lowering cardiovascular problems (Yusuf et al., 2000).

Pharmacokinetics: The liver converts oral ramipril to their active metabolite, ramiprilat. Ramipril's 13–17-hour terminal half-life and 50–60% oral bioavailability allow once-daily blood pressure management (Goodman & Gilman, 2018). Ramipril and its metabolites are mostly eliminated by the kidneys, thus renally impaired patients should take less (Katzung, 2021).

2)Losartan

Losartan is an angiotensin II receptor blocker that inhibits the AT_1 receptor. Inhibiting angiotensin II–mediated vasoconstriction, aldosterone production, salt retention, and sympathetic nervous system activation lowers primary hypertension patients' systemic blood pressure (Burnier, 2001). Losartan does not degrade bradykinin like ACE inhibitors, reducing dry cough and angioedema risk (Messerli et al., 2018). Oral losartan is well-absorbed and metabolized by CYP2C9 and CYP3A4, resulting in the active metabolite EXP3174, which has more AT_1 receptor-blocking effect than the parent drug (Burnier, 2001).

Side Effects of Ramipril and Losartan

Both medications are well-tolerated and do not impact potassium, liver enzymes, or renal function (Kiran et al., 2010). However, class-specific side effects arise : 1) Ramipril: Bradykinin

metabolism-related ACE inhibitors induce 18.3% dry cough (Alam et al., 2021). 2) Losartan: Essential for ACE inhibitor cough failure but may induce dizziness (10%) (Alam et al., 2021). 3) Losartan boosts insulin sensitivity and adipose tissue activity, whereas Ramipril has no metabolic impact (Derosa et al., 2011).

Recommended Use for Hypertension with Complications

Medicine selection should reflect patient issues : 1) Losartan enhances heart failure EF and ventricular reversal remodeling (Alam et al., 2021). For maximal SBP reduction, use ramipril (Alam et al., 2021). 2) Dual blocking (Ramipril and Losartan) decreases cardiac mass and cardioprotects patients with extra LVM better than either drug alone (Argano et al., 2026). 3) Diabetes and High Cardiovascular Risk: Losartan reduces vascular damage and remodeling biomarkers and increases insulin sensitivity (Derosa et al., 2011). 4) Antioxidant-focused patients should take ramipril to boost glutathione and reduce oxidative stress (Kiran et al., 2010).

CONCLUSION

Ramipril and losartan both modulate the renin–angiotensin–aldosterone system to reduce systolic and diastolic blood pressure in patients with primary hypertension, with ramipril potentially providing greater SBP reduction through its dual mechanism of angiotensin II suppression and bradykinin potentiation. Clinical evidence indicates that both drugs achieve similar blood pressure control across patient populations, though ramipril may cause cough and other ACE inhibitor–related adverse effects, while losartan is effective for ACE inhibitor–intolerant patients and may improve insulin sensitivity and adipose tissue function, albeit with dizziness in some cases.

Minor renal, electrolyte, and hepatic side effects occur with both agents, and individualized therapy should consider comorbidities such as diabetes, cardiovascular risk, heart failure, metabolic dysfunction, or oxidative stress. Treatment selection may also be guided by specific therapeutic goals, such as SBP reduction or prevention of left ventricular hypertrophy through monitored RAAS inhibition. Given the heterogeneity in existing studies, future research should focus on well-designed, head-to-head trials and systematic reviews comparing ramipril and losartan across primary hypertension subgroups to optimize personalized treatment strategies.

REFERENCES

Alcocer, L. A., Bryce, A., Brasil, D. D. P., Lara, J., Cortes, J. M., Quesada, D., & Rodriguez, P. (2023). The pivotal role of angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers in hypertension management and cardiovascular and renal protection: A critical appraisal and comparison of international guidelines. *American Journal of Cardiovascular Drugs*.

Aqilla, R. S. (2025). Pemberian diet DM RG pada pasien dengan radiculopathy, diabetes mellitus, essential hypertension, spondylosis, spinal stenosis. *Jurnal Ilmu Kesehatan*.

Bruyn, E., Nguyen, L., Schutte, A., Murphy, A., Perel, P., & Webster, R. (2022). Implementing single-pill combination therapy for hypertension: A scoping review of key health system requirements in 30 low- and middle-income countries. *Global Heart*.

Brunström, M., & Carlberg, B. (2018). Association of blood pressure lowering with mortality and cardiovascular disease across blood pressure levels: A systematic review and meta-analysis. *JAMA Internal Medicine, 178*(1), 28–36.

Burnier, M., & Egan, B. M. (2019). Adherence in hypertension. *Circulation Research, 124*(7), 1124–1140.

Campbell, K. N., Pennese, N., Zaffalon, A., Magalhaes, B., Faiella, M., Caster, D. J., Radhakrishnan, J., Tesar, V., & Trachtman, H. (2022). Efficacy and safety of ACE inhibitor and angiotensin receptor blocker therapies in primary focal segmental glomerulosclerosis treatment: A systematic review and meta-analysis. *Kidney Medicine, 4*(5), 100457.

Chen, R., Suchard, M. A., Krumholz, H. M., Schuemie, M. J., Shea, S., Duke, J., Pratt, N., Reich, C. G., Madigan, D., & You, S. C. (2021). Comparative first-line effectiveness and safety of ACE (angiotensin-converting enzyme) inhibitors and angiotensin receptor blockers: A multinational cohort study. *Hypertension, 78*(3), 591–603.

de Boer, I. H., Khunti, K., Sadusky, T., & Tuttle, K. R. (2022). Clinical practice guidelines to synthesize data and provide expert direction on diagnosis and treatment. Guidelines must be evidence-based,

systematic, transparent. *Diabetes Care*.
Ettehad, D., et al. (2016). Blood pressure lowering for prevention of cardiovascular disease and death: A systematic review and meta-analysis. *The Lancet, 387*(10022), 957–967.
Hiremath, J., Kirpalani, A., Chafekar, D., & Jayagopal, P. B. (2026). Hypertension management beyond blood pressure control in India: An expert consensus on angiotensin II receptor blocker and calcium channel blocker. *Cureus*.
Le, N. N., Frater, I., Lip, S., & Padmanabhan, S. (2025). Hypertension precision medicine: The promise and pitfalls of pharmacogenomics. *Pharmacogenomics*.
Messerli, F. H., Bangalore, S., & Bavishi, C. (2018). Angiotensin-converting enzyme inhibitors in hypertension. *Journal of the American College of Cardiology, 71*(13), 1474–1482.
Mills, K. T., et al. (2020). Global disparities of hypertension prevalence and control. *Circulation, 141*(9), 777–793.
Rahman, A. R. A., Magno, J. D. A., Cai, J., Han, M., Lee, H. Y., Nair, T., Narayan, O., Panyapat, J., Van Minh, H., & Khurana, R. (2024). Management of hypertension in the Asia-Pacific region: A structured review. *American Journal of Cardiovascular Drugs*.
Smolińska, S., Antolín-Amérigo, D., & Popescu, F.-D. (2023). Bradykinin metabolism and drug-induced angioedema. *International Journal of Molecular Sciences*.
Taddei, S., & Bortolotto, L. A. (2016). Unraveling the pivotal role of bradykinin in ACE inhibitor activity. *American Journal of Cardiovascular Drugs*.
Valerio, G., Di Bonito, P., Calcaterra, V., Cherubini, V., Corica, D., de Sanctis, L., Di Sessa, A., Faienza, M. F., Fornari, E., Iughetti, L., Licenziati, M. R., Manco, M., del Giudice, E. M., Morandi, A., Salerno, M., Street, M. E., Umano, G. R., Waśniewska, M., & Di Bonito, P. (2024). Cardiometabolic risk in children and adolescents with obesity: A position paper of the Italian Society for Pediatric Endocrinology and Diabetology. *Italian Journal of Pediatrics*.
Wei, Q. (2024). Study on drug optimization for patients with comorbid hypertension and coronary heart disease. *Journal of Food and Drug Safety Research*.
Williams, B., et al. (2018). 2018 ESC/ESH guidelines for the management of arterial hypertension. *European Heart Journal, 39*(33), 3021–3104.
Xie, X., et al. (2020). Comparative effectiveness of renin–angiotensin system inhibitors. *BMJ, 368*, m193.